

**REMARKS/ARGUMENTS**

Recitation of the Markush group of diseases introduced by previous amendment has been deleted, and the claims have been directed to Parkinson's disease, as previously specified in claim 50. Prophylactic claims have also been amended to recite that the patient is at known genetic risk of the disease as supported by e.g., paragraph 133. Dependent claims rendered redundant by these amendments have been cancelled. Support for the new claims is provided by e.g., paragraph 134. No amendment should be construed as acquiescence in any ground of rejection. Applicants use the paragraph numbering of the specification in responding to the Examiner's comments.

9. Claim 78 has been cancelled.

10. Claims 41, 42, 45, 47, 48, 71, 72, 75, 77 and 78 stand rejected for obviousness type double patenting over various Schenk patents (of record) and Kotzbauer et al. Applicants disagree with the basis for the rejection but have mooted in by introducing the element of claim 50 into the independent claims. Claim 50 was not subject to rejection on this basis.

11. Claims 41-46, 48 and 50-55 stand rejected under 35 USC 112, first paragraph on the basis that the term "therapeutically treating" includes a complete cure, which is alleged not to exist. Likewise claims 71-76 and 78-80 stand rejected on the basis that they encompass complete prevention, which is also alleged not to exist.

Assuming *arguendo* that the claimed methods cannot completely prevent or cure a Lewy body disease, they would be no different than treatment with many other highly successful drugs. For example, it is well known that the success of "blockbuster" cancer drugs is measured in increments of extending the life of a patient for a few months, a result far removed from total cure or prevention. In these circumstances, applicant submits that in the presently claimed methods as in other patents claiming methods of treatment or prophylaxis, the possibility that the methods may not achieve a total cure or prevention is not detrimental to enablement and need not be excluded from the claims. Enablement does not require that generic claims function

in every conceivable circumstance. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 USPQ 409 (Fed. Cir. 1984).

In the event that Examiner persists with this rejection, applicants also request clarification from the Examiner if any alternative language in the claims would address his concerns. For example, the concept of prophylaxis could also be recited in terms of delaying or inhibiting onset of a Lewy body disease in a patient susceptible to the disease, and therapeutic treatment could be expressed simply as treatment of a patient suffering from a Lewy body disease. Alternatively, it would appear that the Examiner is seeking language that explicitly excludes the possibility of total cure or prevention. If the latter, applicant respectfully submits that this is an unreasonable requirement that is rarely, if ever, insisted on in patents claiming methods of treatment or prophylaxis notwithstanding that the capacity of such methods to effect total cure or prevention of a disease would almost always be, at best, unknown.

All claims also stand rejected for lack of enablement on the basis that the term Lewy body disease encompasses at least 18 different diseases, with different characteristics. The Examiner alleges that it is not known which LBD diseases other than those co-presenting with AD the claimed invention would be useful for. The Examiner also alleges that the present inventors own paper states that it is not known whether antibody treatment results in behavioral or cognitive improvements. The Examiner also alleges that the transgenic mice expressing alpha synuclein are models of Parkinson's disease but not other Lewy body disease. The Examiner also alleges the specification does not exemplify passive treatment. Finally, the Examiner quotes from the inventors paper that "further development of this approach might have a potential place in treatment" as indicating present lack of enablement. These remarks will be addressed in turn.

The Examiner's comments regarding there being several distinct Lewy body diseases are moot in view of amendment of the claims to recite Parkinson's disease.

The Examiner's comment that the skilled person would not know which LBD disease other than those with concomitant Alzheimer's disease to administer the claimed method appears to overlook the results presented in Example VI (p. 63 et seq.). As discussed above, this example shows that treatment with A $\beta$  reduces synuclein deposits in both mice with a synuclein transgene and mice with dual double APP and synuclein transgenes. That A $\beta$  treatment can

reduce synuclein deposits even in the absence of accumulation of A $\beta$  resulting from an APP transgene, suggests that the claimed methods are useful on Lewy body patients lacking concomitant Alzheimer's disease.

Insofar as the rejection is based on provision of working examples for active immunization but prophetic examples for passive rejection, the Examiner's position on enablement is inconsistent with that on obviousness. At p. 10 of the office action the Examiner takes the position that "because induction of antibodies is the goal of vaccination with peptides, and thus the artisan would expect similar success from administering an antibody."

Finally, it is respectfully submitted that the Examiner is making too much of certain remarks in the inventors' own paper. Although one sentence in the paper begins by saying it is unclear whether the amelioration of neurodegenerative pathology is accompanied by the improvement of behavioral deficits, the sentence concludes by saying that experiments are underway to assess this possibility. One would expect that a treatment that ameliorates the major pathological feature of Lewy body disease (i.e., synuclein deposits) would have at least some benefits on symptomatic aspects of the disease resulting from the pathology. Likewise, the paper's comments regarding further developments of the approach described having a potential place in treatment of LBD should be understood in the typical context of drug development. The average time between first discovery of a drug and marketing approval is thirteen years. Of necessity, most patent applications on drugs and method of treatment are filed early in the process before any public disclosure has occurred. The requirements under the law for obtaining a patent are not as stringent as the requirements for obtaining government approval to market a particular drug for human consumption. *In re Brana*, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995). "Testing for full safety and effectiveness. . .is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings." *Id.* Thus, the mention of further development before a treatment is available is not inconsistent with enablement.

For these reasons withdrawal of the rejection is respectfully requested.

12. Claims 41, 42, 44, 45, 46, 48, 50, 51-53 54, 5, 71 74 and 75 stand rejected as allegedly anticipated by US 2002/0187157 and US2003/00086938 [Jensen applications}. In the previous response, applicant noted the following.

Jensen is mainly directed to administration of A $\beta$  for the treatment of Alzheimer's disease. Jensen also mentions other "Alzheimer-like" diseases, including Parkinson's, Huntington's and prion-related diseases (*see* paragraph 247). However, Jensen does not disclose that the very same treatment for Alzheimer's disease (namely administration of A $\beta$ ) should also be given to the other diseases mentioned. Insofar as one can determine what Jensen is proposing, it would appear more likely he is proposing that other diseases be treated not with A $\beta$ , the major peptide associated with Alzheimer's disease, but with whatever peptide plays a comparable role in the disease in question.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case based upon the prior art (*In re Piasecki*, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984)). Here, the cited reference refers separately to A $\beta$  and Parkinson's disease but never in the same sentence or paragraph or otherwise in a manner that clearly conveys an intent to administer A $\beta$  for the treatment of Parkinson's disease. As discussed above, it is in fact unlikely that this was what Jensen intended. However, insofar as there is doubt on this issue, the doubt should inure to the benefit of the applicant given that the burden of proof rests with the Patent Office.

The office action's characterization of the above as an argument that the Jensen application do not intend to treat disease such as Parkinson's is incomplete. Applicants' position is in fact that the Jensen applications do not evidence a clear intent to treat diseases, such as Parkinson's, *with AB or an antibody thereto*.

The Examiner next draws applicants attention to a sentence in the Background saying that Parkinson's disease is an amyloid associated disease. It is not disputed that the Jensen publications so characterize Parkinson's disease. What is at issue is how they propose to treat it. This sentence in the background does not address this issue.

Next the Examiner points applicants to claims 34 and 22 of US 2002/0187157. Claim 34 is directed to a method of treating a genus of diseases characterized by amyloid

deposits. Claim 22, from which claim 34 depends, specifies a Markush group of about fifty peptides, one of which is A $\beta$ . In combination, claims 34 and 22 are directed to treating a broad genus of diseases with a Markush group of fifty or so agents. Such a combination probably includes over a thousand combinations of diseases and agents.

Description of genus having so many potential combinations, the vast majority of which are not individually described does not compensate for the ambiguity discussed in the previous response in which it was noted that although A $\beta$  and Parkinson's disease were mentioned separately, they were never discussed in the same sentence or paragraph or otherwise in a way that clearly conveyed an intent to treat Parkinson's disease with A $\beta$ . A description of broad genus is insufficient to provide written description of each and every individual member within that genus. *In re Ruschig*, 154 USPQ 118 (CCPA 1967). "Not having been specifically named or mentioned in any manner, one is left to select from the myriads of possibilities encompassed by the broad disclosure with no guide indicating or directing that this particular compound should be made rather than any of the many others which could also be made."

Insofar as some patients with Parkinson's have concurrent Alzheimer's, and the cited publications discuss treatment or prevention of Alzheimer's disease with A $\beta$ , the present claims are directed to a species that partly overlaps the genus of the cited art. The MPEP states that provided a species is not clearly named in the cited art, it can be both novel and nonobvious over the genus, particularly when there is evidence of an unexpected result within the species (MPEP 2131.03). Here, there is evidence that treatment with A $\beta$  or antibodies thereto provides an unexpected result in for patients having both a disease characterized by amyloidogenic deposits of A $\beta$  and Parkinson's disease. Example VI (p. 63 et seq.) shows that treatment with A $\beta$  reduces synuclein deposits in mice with just a synuclein transgene, and reduces both deposits of A $\beta$  and synuclein in mice with a mice with a dual double APP and synuclein transgenes. That A $\beta$  treatment can reduce both deposits of A $\beta$  and synuclein deposits indicates that A $\beta$  (or an antibody thereto) is effective against both diseases in patients having both Parkinson's disease and a disease characterized by extracellular deposits of A $\beta$ . That A $\beta$  is effective against the Lewy body disease in patients having both diseases represents an unexpected result.

For the reasons discussed above, that claims constitute a species of a prior art genus is not sufficient for obviousness. Claims directed to a species not specifically named and associated with an unexpected result are not obvious over the genus.

A similar analysis applies to claim 27 of US 2003/0086938. This claim is directed to a method of treating or preventing a genus of Alzheimer's disease or other disease and conditions characterized by A $\beta$  deposits by downregulating A $\beta$  or APP. Assuming *arguendo* that some patients with Parkinson's disease constitute a subset of the specified genus, and that methods of downregulating A $\beta$  include administration of A $\beta$ , the claim still provides no specific disclosure of the combination of treating Parkinson's disease with A $\beta$ . That claims are directed to a subgenus that in part overlaps a cited art genus is not sufficient for anticipation or obviousness. When the claims encompass only a species of the genus and are associated with an unexpected result, the claims are neither anticipated nor obvious over the genus.

The Examiner is also requested to consider the patentability of claims 54, 55 and 81-84 directed to methods of treatment or prophylaxis of patients free of Alzheimer's disease or patients free of clinical symptoms of amyloidogenic diseases characterized by extracellular amyloidogenic deposits. The cited Jensen applications provided no specific disclosure connecting treatment with A $\beta$  or antibodies thereto with such patients free of Alzheimer's disease or free of clinical symptoms of diseases characterized by extracellular amyloid deposits. Although the Jensen applications might evidence an intent to treat Parkinson's patients, they do not distinguish between Parkinson's patients with or without concurrent Alzheimer's disease. Thus, the Jensen publications provide no specific disclosure of the classes of patients to which claims 54, 55 and 81-84 are directed, much less a clear intent to treat such patients with A $\beta$  or an antibody thereto.

Claims 44 and 74 are further distinguished in that the Jensen applications do not provide specific disclosure of methods in which a combination of A $\beta$  or antibody thereto and alpha synuclein or an antibody thereto are administered. Although the Jensen publications may generally refer to using at least one amyloidogenic polypeptide or subsequence thereof, the publications list many examples of such polypeptides, and do not disclose the specific combination of A $\beta$  and alpha synuclein.

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For all these reasons, withdrawal of the rejection is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

  
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